

Knowledge and attitudes of adolescents towards the human microbiome and antibiotic resistance: a qualitative study

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Background: Antibiotic and dietary behaviour affect the human microbiome and influence antibiotic resistance development. Adolescents are a key demographic for influencing knowledge and behaviour change.

Objectives: To explore adolescents' knowledge and attitudes towards the microbiome and antibiotic resistance, and the capability, motivation and opportunity for educators to integrate microbiome teaching in schools.

Methods: Qualitative study informed by the Theoretical Domains Framework (TDF) and COM-B model. Six educational establishments were purposively selected by rural/city and socioeconomic status, within Gloucestershire, South West England in 2019. Forty 14–18-year olds participated in focus groups, and eight science or health educators participated in interviews. Data were analysed thematically, double-coded and mapped to the TDF/COM-B.

Results: Adolescents were aware of 'good microbes' in the body but lacked deeper knowledge. Adolescents' knowledge of, and intentions to use, antibiotics appropriately differed by their levels of scientific study. Adolescents lacked knowledge on the consequences of diet on the microbiome, and therefore lacked capability and motivation to change behaviour. Educators felt capable and motivated to teach microbiome topics but lacked opportunity through absence of topics in the national curriculum and lack of time to teach additional topics.

Conclusions: A disparity in knowledge of adolescents needs to be addressed through increasing antibiotic and microbiome topics in the national curriculum. Public antibiotic campaigns could include communication about the microbiome to increase awareness. Educational resources could motivate adolescents and improve their knowledge, skills and opportunity to improve diet and antibiotic use; so, supporting the UK antimicrobial resistance (AMR) national action plan.

Introduction

Changing human lifestyles and societal norms are impacting the human microbiome and contributing to poorer health in the population.¹ The use of antimicrobials, especially antibiotics, diminishes variation in the microbiome² and contributes to the spread of antimicrobial resistance (AMR), one of the biggest public health threats facing the world.³ Microbiome research and medicine continues to expand, including personalized probiotics and prebiotics, personalized diets and faecal microbiota transplantation (FMT).⁴

Public knowledge and attitudes around the role of the microbiome in health and wellbeing has not yet been investigated, and there may be potential to improve appropriate use of antimicrobials and other lifestyle behaviours through education on the

microbiome. UK household surveys across the last decade suggest a continued misunderstanding of the effect of antibiotics and hygiene on the microbiome and immune system.^{5,6} Current antimicrobial stewardship (AMS) campaigns and education of the public, including children,^{7–11} do not feature messages on the adverse effect of antimicrobials on the microbiome. It is unclear how microbiome information through media, products (such as dietary supplements), and advertisements are affecting public behaviour and attitudes, if at all.

The UK 5 year action plan for AMR highlights the important role of children and adolescents and aims to improve education so that young people leave school with the knowledge and skills to prevent infection and emergence of AMR.¹² Adolescents are a

neglected demographic for behaviour change towards antibiotics; this is concerning as European population surveys and UK household surveys continually show adolescents to have the poorest knowledge of appropriate antibiotic use.^{5,6,13-16} Qualitative research grounded in behavioural theory is needed to understand how to best intervene to improve behaviour. One qualitative study with English adolescents (16–18 years) found lack of concern for antibiotic resistance, and potentially damaging beliefs about antibiotic use.¹⁷ Furthermore, Eley et al.¹⁸ found English school students (7–16 years) lacked knowledge of the effects of antibiotics on beneficial bacteria in the body. Adolescents are a key demographic for education around improved diet as their fruit and vegetable intake is very low;¹⁹ therefore behaviour change interventions around the microbiome have the potential to impact multiple areas of public health to benefit adolescents. Adolescents may be exposed to information on the microbiome in schools as well as through media and adverts and full-time education offers opportunity for improved health education, especially with statutory health education introduced in England in 2020.²⁰

Behavioural models provide a theoretical lens for researchers to explore facilitators and barriers to desirable behaviours and identify where intervention can effect change.²¹ The Theoretical Domains Framework (TDF) was developed to understand implementation of evidence-based practice and behaviour change in healthcare professionals through amalgamating 33 theories into 14 domains to explain influencers of behaviour.²²⁻²⁴ It is often used in health research with patients, the public and young people.^{22,25} The TDF fits into the COM-B model, which is at the centre of the behaviour change wheel. COM-B looks at behaviour in terms of Capability, Opportunity and Motivation and is often used in conjunction with the TDF for intervention design.²¹

This study aimed to investigate 14–18-year-old adolescents' knowledge and attitudes towards the human microbiome and antibiotic resistance and explore educators' capability, motivation and opportunity to embed microbiome teaching in English schools.

Methods

Study design

Focus groups and semi-structured interviews with adolescents and educators, respectively, were conducted in secondary school settings in Gloucestershire, South West England. The TDF and COM-B model (Figure 1) were used in the design of interview questions (see [Supplementary data](#), available at JAC-AMR Online) and analysis of data to identify factors that influence behaviours.^{22,24} The authors have backgrounds in public health, microbiology and behavioural science. Microbiome researchers were consulted on the focus group and interview schedules and recommended topics on diet and the use of antibiotics and to discuss a 2018 news article on FMT.²⁶ The topic guides were piloted and discussed with a secondary school biology educator and an adolescent studying A-Level Biology. We adhered to consolidated criteria for reporting qualitative research (COREQ) in this report as described in Table S1.

Setting and participants

We recruited adolescents via schools as we considered this to be the most efficient method. The county of Gloucestershire was close to the lead researcher's base and had variation in socioeconomic status, rural and urban areas and school types. Purposive sampling aimed to recruit schools with a range of different characteristics via a three-stage method (Figure 2). A list of secondary schools from the Department for Education²⁷ were stratified by urban/rural setting (defined as schools within and outside the main towns, respectively) and then by an index multiple deprivation (IMD) as a measure of socioeconomic status.²⁸ Schools in each stratum



COM-B component		TDF Domain
Capability	Psychological	Knowledge
		Skills
	Physical	Memory, Attention and Decision Processes
		Behavioural Regulation
Opportunity	Social	Skills
	Physical	Social Influences
Motivation	Reflective	Environmental Context and Resources
		Social/Professional Role & Identity
		Beliefs about Capabilities
		Optimism
	Automatic	Beliefs about Consequences
		Intentions
		Goals
		Social/Professional Role & Identity
		Optimism
		Reinforcement
		Emotion

Figure 1. COM-B model and Theoretical Domains Framework (TDF). Adapted from Figures 1 and 2 in Michie et al.²⁴

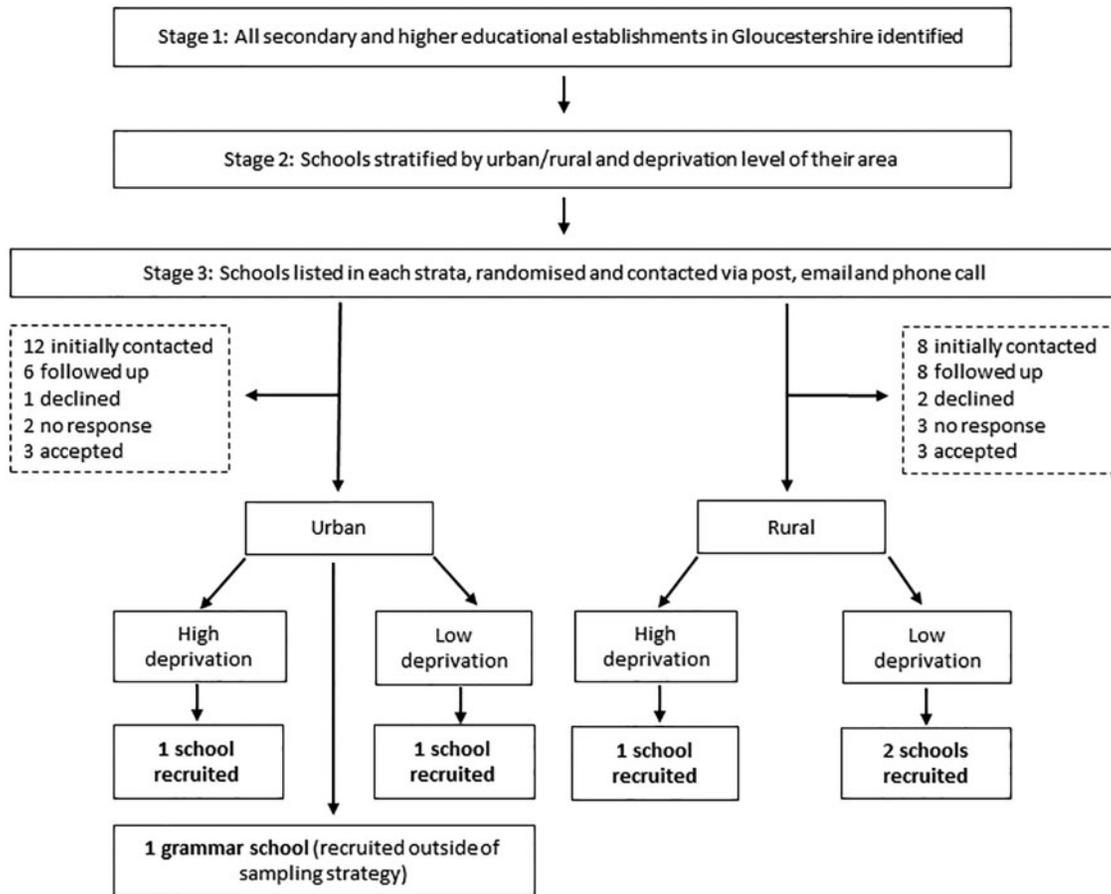


Figure 2. Purposive recruitment strategy for educational establishments.

were listed, randomized using Microsoft Excel random number function and contacted from the top of the list. Additionally, a grammar school (a state school that selects its pupils by entrance exam) was recruited outside of the sampling frame.

Of 20 schools contacted, 6 accepted, 11 did not respond and 3 declined (due to a lack of time or on-going examinations). None of the recruited schools dropped out following agreement to participate. Five of the six schools had a further education sixth form (for adolescents aged 16–18 years). Schools were asked to invite participants for two separate focus groups with adolescents studying General Certificate Secondary Education (GCSE) (14–16 years) or A (advanced)-Level (16–18 years). Due to the need to receive parental consent from participants under the age of 16 years, educators were asked to select and invite adolescent participants prior to data collection and standard guidance was given to select a varied sample of adolescents. Schools were invited to nominate at least one educator who teaches a science or health subject to adolescents aged 14–18 years for an interview.

Data collection

Interviews and focus groups took place between May and July 2019 in a private room of each school and lasted 40–60 minutes. Adolescent focus groups had between three and six participants. Educators took part in interviews and one dual interview. Ground rules, including not sharing information outside of the group were agreed. Data were collected by two experienced qualitative female researchers (C.V.H. and C.V.E.). Neither were

familiar with the participants. Researchers made field notes and recorded demographic information from participants, including subjects they taught/studied. Data collection continued until the researchers agreed that data saturation was reached, and no new themes were emerging.²⁹ Discussions were recorded and stored on a secure PHE server in accordance with Data Protection Act 2018 and General Data Protection Regulations (GDPR). Files were anonymized, transcribed by an external agency and checked for accuracy (by C.V.H.). Educators were provided with a £20 high street voucher and adolescents received a certificate of participation.

Data analysis

Data analysis by C.V.H. aimed to provide a detailed account of the dataset via an inductive six-stage thematic analysis.³⁰ NVivo (version 11) software was used to support analysis, which included labelling data with semantic patterns and meanings using the language inherent in the data. C.V.E. completed coding of 20% of the data, and discussions between the researchers resolved any differences. Codes were organized into themes which were then mapped to the theoretical models. For reporting, the research team agreed that the TDF was appropriate for the larger adolescent dataset which explored multiple behaviours related to the microbiome.²² The research team agreed the COM-B²⁴ was more appropriate for reporting the educator data set, which was less detailed and aimed to explore a single behaviour (integrating teaching of the microbiome). No repeat interviews were completed, and participants did not provide feedback.

Ethics

National Research Ethics Service approval was not required, in accordance with their guidelines.³¹ Ethics approval was provided by the Cardiff University School of Medicine Research Ethics committee (SMREC Reference Number: 19/34) and internally reviewed by PHE Research Ethics and Governance Group (REGG) (Reference: R&D 360). All participants provided informed consent and had opportunity to ask questions prior to interviews commencing. A signed guardian permission form was obtained for adolescents under the age of 16 years.

Results

Participant characteristics

Forty adolescents and eight educators participated in the study from six schools (Table 1). Twenty-two (55%) adolescents were aged 14–16 years, and 18 (45%) were aged 16–18 years. Educators taught a range of subjects, notably science GCSE ($n = 6$) and A-Level Biology ($n = 4$) and six had at least one Bachelor of Science degree.

Emerging themes of adolescents

Adolescent themes, TDF mapping and illustrative quotes are summarized in Table 2 (full quotes in Table S2).

Knowledge of the microbiome and antibiotics (TDF: knowledge)

All adolescents displayed a basic awareness of the existence of microbes in the body. Most referenced ‘good microbes’ but lacked knowledge on their role and confused them with antibodies and enzymes. Adolescents (16–18 years) studying biology A-Level had better knowledge of antibiotics than other adolescents, who commonly stated antibiotics could treat viruses or confused antibiotics with other medicines. Most adolescents, besides those studying biology A-Level, did not understand the concept of antibiotic resistance, which they confused with drug addiction or dependency and some discussed how taking antibiotics could weaken the immune system as it was relying on medicine to fight an infection.

Negative consequences of taking antibiotics (TDF: Beliefs about consequences, emotions)

Some adolescents stated that antibiotics killed ‘good bacteria’ in the body which could lead to ill health, digestive issues and a weakened immune system. Adolescents studying biology A-Level reported that taking antibiotics could cause antibiotic resistance and that this would lead to certain illnesses being untreatable. Some reported that specific behaviours, such as not taking the full course of antibiotics, would increase antibiotic resistance.

Table 1. Adolescent and educator characteristics

Characteristic	Adolescents ($n = 40$)		Characteristic	Educators ($n = 8$)	
	Number (%)			Number	
Gender			Gender		
Male	18 (45)		Male		2
Female	22 (55)		Female		6
Age range, years			Subjects taught		
14–16	22 (55)		Science GCSE		6
16–18	18 (45)		PSHE		2
Subjects studied			Food science GCSE		1
GCSE triple science	18 (45)		Biology A-Level		4
GCSE double science	4 (10)		Other science A-Level		1
A level Biology	10 (25)		Health and social care BTEC		2
A level non-Biology	5 (13)		Qualifications held (bachelor or master degree)		
Health and Social Care	3 (7)		Biology or microbiology		5
			Other science degree		1
			Food or nutrition degree		1
			No science degree		2
School location			School location		
Urban	16 (43)		Urban		3
Rural	23 (57)		Rural		5
Socioeconomic status of location ^a			Socioeconomic status of location ^a		
High	16 (40)		High		3
Low	24 (60)		Low		5

GCSE, General Certificate of Secondary Education; BTEC, Business and Technology Education Council; PSHE, Personal, Social, Health and Economic Education; A-Level, Advanced Level.

Note. In England, GCSE triple science is a route allowing students to study biology, chemistry and physics as separate subjects. GCSE double science is a route where students study biology, chemistry and physics in one subject, awarded with two GCSEs.

^aSocioeconomic status relates to the Index of Multiple Deprivation (IMD) of the school postcode.

Table 2. Adolescent themes and subthemes linked to TDF

Theme (TDF domain)	Subtheme	Quote
Knowledge of the microbiome and antibiotics (Knowledge)	The microbiome	Participant 1: So, the good one's help keep you healthy and the bad ones make you not healthy, they make you sick. . .
	Positive role of microbes in the body Antibiotics and antibiotic resistance	Participant 2: They try and kill the bad ones. Participant 3: With the digestive ones, I feel like those microbes can digest the things that maybe your body can't. <u>School C, pupils aged 16–18 years</u>
Negative consequences of taking antibiotics (Beliefs about consequences, Emotions)	Side effects of antibiotics on the microbiome	Participant 2: It [antibiotics] gets rid of the bad but in effect, it also takes away some of your good microbes.
	Taking antibiotics can lead to antibiotic resistance	Participant 3: So, it lowers your immune system in a way.
	Consequences of antibiotic resistance	Participant 2: So, would it mean you're more vulnerable to getting another virus or bacteria? <u>School F, pupils aged 14–16 years</u>
Behaviours that affect the microbiome (Beliefs about consequences)	Hygiene	Participant 1: I think the whole bleaching everything, keeping everything clean, sterilizing everything all the time, washing three times a day, doesn't really build up an immune system that way.
	Eating food containing live cultures of microbes	<u>School C, aged 16–18 years</u>
	Consequences of not protecting your microbiome	
Barriers to behaviours that affect the microbiome (Beliefs about capabilities, Environmental context and resources)	Perceived lack of knowledge	Participant 1: No clue what good microbes are so if we maybe knew about it then we'd probably try and protect them wouldn't we?
	Lack of control over lifestyle	<u>School A, aged 16–18 years</u>
	Lack of resources	
Intentions to engage in behaviours that affect the microbiome (Intentions)	Intentions to change behaviour	Participant 1: Well disposal of them, so if you have antibiotics you need to dispose of them in the correct way. . .
	Intentions to use antibiotics appropriately	Participant 2: Only take them when you really need to. . . something major, well not major, but like tonsillitis and stuff that you can't just take paracetamol for that. It'll probably just get worse and worse, antibiotics is needed for that. It's like say if you've got a sore throat or a cold, you shouldn't get antibiotics, because it's just a waste of it. <u>School B aged 16–18 years</u>
Young people's role in preventing AMR (Social/professional role and identity, social influences)	Role as a consumer of antibiotics	Participant 1: . . . the older generation know that there's an issue, but just leaving it to the next generation along to –
	Perceived generational roles	Participant 2: Climate change, antibiotic resistance. Participant 1: A lot of things that are really going to cause issues for us. . . have just been put, swept under the carpet <u>School D, aged 16–18 years</u>
Beliefs and consequences of FMT (Beliefs about consequences, Emotions)	Perceived benefits of FMT	Participant 1: They might accidentally sneak in some of the bad bacteria. . .
	Perceived risks of FMT	Participant 4: You could be allergic maybe. Participant 1: It would just be rejected and then it could actually be really serious. Participant 4: Then you'd need to take rejection pills and rejection pills are linked to cancer. . . <u>School A, aged 14–16 years</u>

TDF, Theoretical Domains Framework; FMT, faecal microbiota transplantation; AMR, antimicrobial resistance.

Note: Quotes are reported with the age group and school pseudonym.

Adolescents with knowledge of AMR tended to show more concern while others felt it was not relevant to them.

Behaviours that affect the microbiome, barriers and intentions (TDF: Beliefs about consequences, beliefs about capabilities, environmental context and resources, intentions)

Advertisements and media had influenced adolescent's beliefs about the microbiome, including that eating high-fibre foods and

those that contained live cultures of microbes including Yakult, kefir and kombucha would improve digestion. They reported these foods would balance the microbes in the body, either by killing harmful microbes or replenishing 'good microbes'. Some reported being 'too clean' could lead to a weakened immune system due to a lack of microbes in the body.

Adolescents did not intend to change dietary behaviours in relation to their microbiome because they lacked knowledge of the

consequences. Adolescents also felt they lacked control and resources, such as time, to improve their diet and lifestyle. Most adolescents intended to use antibiotics appropriately, including following their doctor's advice and disposing of them correctly. Some reflected that having an awareness of the negative effects of antibiotics on 'good bacteria' meant that they would be more likely to think about alternatives to antibiotic treatment unless they had a serious infection.

Young people's role in preventing AMR (TDF: Social/professional role and identity, social influences)

Adolescents perceived their role in preventing AMR was to be a responsible antibiotic consumer but believed the government and healthcare professionals had more responsibility. Some adolescents believed that their parents and grandparents were not taking antibiotic resistance seriously. Adolescents compared antibiotic resistance to climate change and felt that they could make a difference through protests and increasing awareness through social media.

Beliefs and consequences of FMT (TDF: Beliefs about consequences, emotions)

Most adolescents were not familiar with FMT before discussing the article. Initial reactions included disgust, humour and interest at the concept of the procedure; adolescents also discussed its possible positive and negative effects. Some believed the procedure to be natural and would increase 'good microbes' in the gut. Adolescents views on personally receiving FMT differed. While some stated the procedure was unacceptable to them, others believed that the life-saving nature of the treatment made it tolerable. Adolescents confused the procedure with organ transplantation and believed immunosuppressant medication may be needed. Other risks discussed were that microbes from the transplant may cause infection or mutate.

Emerging themes of educators

Educator themes, COM-B mapping and illustrative quotes are summarized in Table 3 (full quotes in Table S3).

Capability to teach about the microbiome

Educators with a science-based degree had more knowledge of the microbiome, including an awareness of its influence on health. Educators gained their knowledge on the microbiome through media rather than traditional training. Confidence to teach the topic varied depending on qualification and those with a strong subject knowledge felt more confident. Educators who felt less confident to teach the topic believed that resources, further information or training would improve their capability.

Motivation to teach about the microbiome

Educators viewed their professional role as preparing adolescents for their later life and career. This included primarily preparing them for examinations, but also helping to build positive attitudes and behaviours, including encouraging a healthy lifestyle. Educators overall felt that the microbiome would be an important topic to teach adolescents, to promote healthy lifestyles and

correct antibiotic use, and to encourage interest in science and public health. Educators felt that current teaching around microbiology and disease focused on the negative aspects of bacteria rather than focussing on the usefulness of looking after the microbes in our bodies.

Opportunities to teach about the microbiome

Educators believed that microbiome topics could fit into a variety of existing subjects, including science, food science, Personal, Social and Health Education (PSHE) and health and social care. The major barrier was that this topic was not included in the curriculum or exam specifications and time constraints meant that additional topics were difficult to cover, especially at A-Level where there was pressure to ensure students could pass exams. Educators suggested the topic should be included in the curriculum or be taught in PSHE where there is a more flexible curriculum. Educators lacked access to educational resources on the microbiome and requested worksheets, interactive activities, animations and videos.

Discussion

This original qualitative study of adolescents' knowledge and attitudes towards the human microbiome revealed a basic awareness of the positive nature of microbes in the body but found a lack of deeper understanding of the role the microbiome plays in health. Data from educators complemented the findings of adolescents. Educators were motivated and capable, depending on their scientific background, to teach microbiome topics but felt they lacked opportunity in the teaching curriculum, exam board specifications, and availability of educational resources.

Comparison with existing knowledge and recommendations

The microbiome is not a routinely taught topic in English schools and adolescents may be constructing incorrect knowledge, potentially based on incomplete messaging in media and advertising. This is mirrored in the common UK public misconception that pathogen exposure improves people's health by 'strengthening' the immune system.³² British news media coverage has often attributed cleanliness as a major cause of reduced exposure to microbes.³³ Beliefs regarding the effects of being 'too clean' and antibiotics on the strength of the immune system have also been reported for adults³⁴ and adolescents¹⁷ in the UK. Evidence-based educational resources are needed to reverse these commonly held misconceptions around the immune system and improve knowledge of the microbiome and antibiotics.

Hawking et al.¹⁷ also found a disparity in knowledge of antibiotics in those studying A-Level Biology compared with those not. The Department for Education and educational authorities should address this knowledge gap and consider including topics around the microbiome, antibiotics and antibiotic resistance in the curriculum at all levels of education, in science and health education subjects. This also supports the UK 5 year AMR action plan.¹²

The belief that resistance is a dependency of the body has been noted often in the literature with respect to adults across Europe and New Zealand³⁴⁻³⁸ as well as concern for the adverse effects of antibiotics on 'good bacteria'.³⁴ A new finding from our study is

Table 3. Educator themes and subthemes linked to COM-B

COM-B	Sub-theme	Quote
Capability	Knowledge of the microbiome	<i>At this point I wouldn't feel confident [to teach about the microbiome]. But I think if I had. . .some good information, or some nice resources, I've got video clips. . .that would get them interested, and may help to, kind of, confidently talk about it. I think as a biologist it would probably be a bit easier for me, because I know a little bit, and I have that interest. But I think with the right resources and things I'd feel confident teaching it, yeah.</i>
	Source of microbiome knowledge	
	Confidence to teach microbiome topics	
		GCSE Science teacher
Motivation	Responsibilities and goals for teaching students	<i>I think it would, it could potentially, reduce students wanting to have antibiotics prescribed for them if they knew the danger it did to their gut. . . And it could help them to be a bit more healthy really with the foods that they eat.</i>
	Goals for teaching microbiome topics	
	Beliefs about the impact of teaching microbiome topics	
		GCSE Science teacher
		<i>I'd like to think that they could understand that antibiotics aren't some sort of magic pill. . .that they don't necessarily have to take them, that actually if they're feeling unwell, perhaps there were other ways that they could treat themselves other than taking antibiotics and things.</i>
		A-Level Biology teacher
Opportunity	Opportunities to teach in existing school subjects	<i>I think the issue is we pretty much teach to exam now so if it's not in the curriculum it does get missed out. . .and the problem is people do hear the word bacteria and because we talk about antibiotics, we talk about diseases, so the assumption is that all bacteria are bad. But of course we know that there are actually quite a few beneficial microbes that our life would be very difficult or, if not impossible, without.</i>
	Barriers to teaching microbiome topics	
	Need for resources	
		A-Level Biology teacher

COM-B, Capability, Opportunity, Motivation, Behaviour; GCSE, General Certificate of Secondary Education; BTEC, Business and Technology Education Council; PSHE, Personal, Social, Health and Economic Education; A-Level, Advanced Level.

Note: Quotes are reported with the subject the educator taught.

that adolescents believed that awareness of the negative effect of antibiotics on their microbiome could influence their future antibiotic behaviour. The most recent public campaign on antibiotics in the UK 'Keep Antibiotics Working' focused on the importance of following medical advice on antibiotics.³⁹ However, the literature shows that the UK public do not believe antibiotic resistance to be relevant for them.⁶ Public health messaging around the microbiome may improve public understanding of the personal consequences of inappropriate antibiotic use and capitalize on the current interest around the microbiome.

A new finding is adolescents' comparison of antibiotic resistance to climate change, and belief that they could improve awareness through social media. Peer education, which has been shown to improve 11–18-year-olds knowledge and attitudes regarding antibiotics^{40,41} could support this generation of adolescents who are motivated to improve health and sustainability.

Lack of control over lifestyle and diet is a common theme in previous qualitative work with adolescents in the USA and Ireland.^{42–45} No previous study has looked at whether awareness of the effect of diet on the microbiome may influence behaviour. Adolescents lacked knowledge on the consequences of diet on the microbiome, and therefore lacked capability and motivation to change their behaviour; therefore, further work is needed to ascertain whether a public health intervention could influence eating habits.

Although not the primary focus of our study, ours is the first study to explore healthy adolescents' attitudes towards FMT. Previous studies with patients found higher acceptability, in comparison with adolescents in our study, which may be due to their ill state and the perception of FMT as lifesaving.⁴⁶

Previous work with educators has found that the national curriculum and lack of time are barriers to increasing education of hygiene and antibiotic topics.^{47,48} Other research by the authors has found that confidence to teach antibiotic topics differs by UK educators' science background,⁴⁹ and that support and training is needed, also demonstrated in the current study.

Limitations

Our findings reflect knowledge and beliefs of adolescents in one region of England who are likely to have similar exposure to education, cultural and social norms and media; therefore, themes may not reflect those of the larger population, or other countries. Adolescents were sampled from schools and did not include college students or those outside education, who may have different knowledge and attitudes. Due to the nature of the methods, there may have been some acquiescence bias from adolescent participants, so that they appeared to hold more desirable opinions or attitudes, for instance towards antibiotic use. Data collection took

place in the summer months, which meant adolescents may have presented better knowledge than other times of the year because of the effects of revising for exams.

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Transparency declarations

None to declare.

Supplementary data

Supplementary Methods and Tables S1 to S3 are available as Supplementary data at JAC-AMR Online.

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